

Review

Sexual transmission and prevention of the hepatitis viruses A-E and G

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Objectives: To assess current knowledge about the potential for sexual transmission of the hepatitis viruses A-E and G and how to prevent any such transmission.

Method: A search of published literature identified through Medline 1966–June 1998 (Ovid v 3.0), the *Cochrane Library* and reference lists taken from each article obtained. Textword and MeSH searches for hepatitis A, B, C, D, E, G, delta, GB virus, GBV-C were linked to searches under the textword terms sex\$, vaccin\$, prevent\$, and MeSH subheadings, epidemiology, transmission, prevention, and control.

Conclusions: There is evidence for heterosexual transmission of hepatitis B, C, D, and G and homosexual transmission of hepatitis A-D and G. Condoms are an effective method for preventing transmission by penetrative vaginal or anal sex although spread of types A and B are linked also to oro-anal sex. Hepatitis types A and B can be prevented by pre- and post-exposure active or passive immunisation. There is still some uncertainty about appropriate target groups for pre-exposure vaccination, particularly against hepatitis A.

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Introduction

Although hepatitis B has been recognised as a sexually transmitted infection for over 25 years, the status of the other types of viral hepatitis with regard to sexual transmission has been less clearly understood until recently. The purpose of this review is to look at recent developments in our understanding of the risks of sexual transmission of viral hepatitis and how any such transmission may be prevented.

Hepatitis A

This infection is usually transmitted by the faeco-oral route, including contaminated food and water, as well as by close personal contact.¹ As sex often involves prolonged close personal contact, it is likely to be associated with transmission of hepatitis A. However, to be classified as a sexually transmitted disease it is necessary to demonstrate that the sexual act itself leads to more spread of hepatitis A than would have occurred in similarly intimate but non-sexual situations. For heterosexual contact there is no such evidence. For instance, in a Canadian study of non-immune household contacts of adult patients with acute hepatitis A, the rate of acquisition of infection in spouses was lower than the rate in children (50% v 77%).² However, there is increasing evidence that male homosexual contact can lead to sexual transmission. This evidence comes mainly from outbreaks. For instance, 210 homosexual men were infected in Melbourne in 1991, constituting 52% of all male cases for that year.³ Similar outbreaks have also been reported in other large cities including London, New York, and Amsterdam.^{4–6} Compared with matched controls, acquisition of hepatitis has been associated with visits to saunas and darkrooms,⁶ sex with anonymous partners in the past 6 weeks, group sex, oro-anal and digital-rectal

intercourse,⁵ and number of partners.^{7–8} Outbreaks have not been confined just to single large cities. An increase in incidence has been observed in homosexual men over the past 4 years (1995–8) in south east England amounting to approximately 100 extra cases per year.^{9–10}

There is therefore evidence that homosexual men can be at increased risk of infection in outbreaks and this increased risk is related to their sexual lifestyle. Is this evidence enough to warrant a change to the universal vaccination of homosexual men? The Department of Health in England and its other UK counterparts unhelpfully advocates vaccinating homosexual males “whose sexual behaviour is likely to put them at risk”, but does not define such sexual behaviour.¹¹ However, seroprevalence studies in the United Kingdom, United States, and Spain all show that the proportion of homosexual men attending centres for sexually transmitted diseases with evidence of past infection (IgG positive) is no higher than that in heterosexual men.^{8–12–13} This suggests that the majority of homosexual men are not at increased risk. The Communicable Diseases Surveillance Service (CDSC) for England and Wales (Thames Region) is coordinating an investigation of an apparent outbreak of hepatitis A in homosexual men which may help to inform debate regarding vaccination policies for hepatitis A. Certainly, human normal immunoglobulin should be offered to anyone in close contact with someone in the infectious phase of hepatitis A (2 weeks before and 1 week after the onset of jaundice) in the previous 2 weeks, regardless of their sexuality.^{11–14} This may be combined with hepatitis A vaccine which, after booster doses, leads to immunity in 95% and lasts 3–10 years or more.^{11–15} The combined hepatitis A and B vaccine (a mixture

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of standard hepatitis A and B vaccines) seems to be equally effective but is given in three doses at 0, 1, and 6 months.¹⁶ There is no evidence that HIV positive individuals are more susceptible to infection or have more severe disease, but they do respond less well to the vaccine in terms of antibody production (73–88%) and with lower antibody titres.¹⁷

Given that the majority of homosexual men do not seem to be at increased risk of hepatitis A there seems to be little justification for vaccinating all homosexual men. There may be a case for vaccinating men with multiple anonymous partners (more than one in 6 weeks), especially with a history of sex in saunas or darkrooms and involving oro-anal (oral role) and digital-rectal (digital role) intercourse,⁵⁻⁸ particularly during an outbreak. This should become clearer after the CDSC study. Many sexually transmitted disease clinics see significant numbers of injecting drug users and there is evidence to suggest that this group is also at increased risk of hepatitis A and therefore should equally be considered for vaccination.^{8,18} Patients who are carriers of hepatitis B or C or have liver disease of another cause may develop severe liver disease after hepatitis A superinfection and should therefore be vaccinated against hepatitis A.¹¹

Hepatitis B

There are several hundred million hepatitis B carriers worldwide, most of whom live in Africa, Asia, and South America.^{19,20} The majority have caught the infection through vertical transmission at birth and horizontal infection of children.²⁰ Other non-sexual routes of infection includes horizontal transmission in institutions for patients with learning difficulties²¹ and parenteral exposure such as occurs among injecting drug users or those infected nosocomially.^{22,23} However, hepatitis B virus is also efficiently transmitted sexually during heterosexual and male homosexual contact.²⁴⁻²⁷

HETEROSEXUAL TRANSMISSION

Several studies have shown that heterosexual transmission is important in female sex workers²⁸⁻³⁰ and their customers³¹ in countries where the prevalence of HBV carriers is high. In one study of Peruvian female prostitutes, 59.8% had evidence of past hepatitis B infection and over the next 3 years the non-immune prostitutes became infected at 4.7% per year, excluding parenteral transmission.²⁸ Evidence of past or current hepatitis B infection was four to six times higher in non-drug using prostitutes than in controls in this and other studies and correlated with number of sexual contacts and sexually transmitted diseases.²⁸⁻³⁰ Outside of prostitution, heterosexual transmission is still important as shown by the 40% transmission rates to non-immune spouses of patients with acute or chronic hepatitis B.^{24,32} There are no clear data on the mechanism of transmission but it is assumed to be unprotected vaginal intercourse. The importance of heterosexual transmission varies from country to country

depending on the background rates of hepatitis B in the heterosexual population, much of it having been acquired by non-sexual routes. Most of the work on female sex workers has been performed in countries where there are a high number of cases and carriers.²⁸⁻³¹ Although the studies provide information on the efficiency of sexual transmission which is generally applicable, they do not provide data on the proportion of infections attributable to sexual transmission in other low prevalence areas. Evidence from the CDSC in England and Wales, countries with a low prevalence hepatitis B carriage (0.01–0.05% in blood donors), shows that heterosexual transmission accounts for only 18% of acute hepatitis B and there is no evidence that transmission to, or by, female sex workers is common.³³ A study in Australia also failed to show prostitution as a risk factor for hepatitis B.³⁴ In the United States, a country of medium prevalence (0.1% blood donors) heterosexual transmission is responsible for almost 30% of infection and has been steadily rising since the early 1980s.²²

MALE HOMOSEXUAL TRANSMISSION

Sexual transmission between homosexual men has been so common and efficient that many of the important hepatitis B vaccination trials in the mid 1970s and early 1980s were performed in this group of people.^{25,26} At that time it was common to find evidence of past infection in 50% or more and HBsAg positive rates of up to 6% in studies of selected groups of homosexual men in the United States and Europe.^{27,35-37} Reported annual incidences of new hepatitis B infection in homosexual men in the United States and elsewhere was 25% or more.³⁸⁻⁴⁰ Transmission of hepatitis B in homosexual men correlates with duration of sexual activity, number of partners, oro-anal and genito-anal sexual contact.^{39,41} Supporting evidence for these routes of infection comes from studies showing hepatitis B virus DNA and surface antigen in semen, saliva, urine, faeces, anal and rectal mucosa in over 50% of samples from hepatitis B carriers.^{42,43} Despite the availability of an effective vaccine, hepatitis B continues to be a significant problem in homosexual men. Studies from the United Kingdom of patients tested in the early 1990s showed that although markers of past infection had fallen to 16–38%, transmission was still occurring as shown by the significant rate of markers in men under 25 years old (6.9%).^{44,45} Furthermore only 33% of STD clinic re-attenders had been vaccinated.⁴⁴ More than 10 years after the introduction of the hepatitis B vaccine the prevalence of hepatitis B markers in a study from America was still 18% in homosexual men under 29 years old.⁴⁶

PREVENTION

There is clear evidence for sexual transmission in both sexes and it seems likely that avoidance of higher risk sexual activity—that is, penetrative anal and vaginal sex and oro-anal sex, would lead to a reduction in transmission rates, particularly when applied to hepatitis B carriers. However, I could find no studies

Table 1 Summary of the types of sexual transmission and methods of prevention of the hepatitis viruses

Virus	Sexual transmission	Prevention of sexual transmission
A	Heterosexual, no evidence	Human normal immunoglobulin for recent (<1 week) contacts Hepatitis A vaccine (primary and post-exposure prophylaxis)
B	Homosexual men, some evidence for oro-anal and digital-rectal sex, especially during outbreaks Heterosexual, probably related to penetrative vaginal intercourse	Condoms, clear evidence in heterosexuals only Hepatitis B specific immunoglobulin, within 7 days of at risk exposure to an infectious case Hepatitis B vaccine, primary* and post-exposure prophylaxis Condoms (some evidence)
C	Homosexual men, genito-anal and oro-anal sex Heterosexual, presumed penetrative vaginal sex Homosexual men, presumed genito-anal sex Transmission rates are low although much higher if the source is HIV infected	
D	Heterosexual, as for hepatitis B Homosexual, as for hepatitis B Occurs as a co-infection with hepatitis B	As for hepatitis B
E	No evidence	None
G	As for hepatitis B Often co-infects with hepatitis B or C	? Condoms No evidence that this virus causes disease.

*Recommended for homosexual men, injecting drug users, and sex workers.

which confirmed that this advice is effective. Condom use has been shown in several studies of female prostitutes to be an effective means of reducing transmission rates of hepatitis B and other STDs.^{47 48} A study of homosexual men did not show self reported use of condoms to be associated with a reduced rate of transmission,⁴⁹ probably as infection would occur as a result of inconsistent condom use and oro-genital sex. Vaccination has a dramatic effect by reducing subsequent infection by almost 100%.^{25 26} Given the high rates of infection, vaccine should be offered to all homosexual men. Unfortunately, despite such a policy for years, vaccine uptake remains disappointingly low,^{44 50} probably because of the extended period of vaccination over 6 months. UK STD clinics favour vaccination of homosexual men, prostitutes, and injecting drug users.⁵¹ In attenders at a central London genitourinary medicine clinic in 1991, evidence of past infection (anti-HBc positive) in heterosexual men was 5.9% and HBsAg carriage less than 0.6%. The figures for women were 3.7% and 0.39%. Anti-HBc prevalence in first time blood donors was 1.1%. The authors suggest that expansion of hepatitis B vaccination to heterosexual attenders at UK genitourinary medicine clinics is not likely to be an efficient means of reducing heterosexual transmission of hepatitis B.⁴⁴ In areas of the world where hepatitis B is more common, universal vaccination is recommended.⁵² The World Health Organisation recommends universal vaccination for all countries but the Department of Health in England has so far not instituted this nor has it indicated that it will.

Hepatitis D (delta virus)

This RNA virus can only exist as a co-infection with hepatitis B. Parenteral transmission is the most important route of infection but this agent can be sexually transmitted. One study in China showed sex with prostitutes to be an important risk factor.⁵³ Other studies have shown sexual transmission of delta virus in both heterosexual and homosexual men.³⁵ As hepatitis D requires concurrent hepatitis B virus infection, it is mainly a significant

population-wide problem in countries where hepatitis B is common. In lower prevalence countries, drug users or their partners account for the majority of cases.⁵⁴ Measures to prevent hepatitis B will also prevent delta virus infection.

Hepatitis C

The subject of sexual transmission of hepatitis C is already being covered in an accompanying review in this issue (p 399) so I will only briefly discuss this topic. Hepatitis C can be sexually transmitted but at a very low rate, probably 0.5–2% per year of a relationship or 5% of all relationships.⁵⁵ Transmission rates are markedly higher if the source patient is also HIV positive.⁵⁵ Condoms are the only adequate protective measure although given the low transmission rate, many people in long term relationships may decline their use.

Hepatitis E

An RNA virus found mainly in developing countries (Indian subcontinent, eastern Europe, Africa, central, and South America), it is transmitted mainly via the faeco-oral route, especially in epidemics associated with contaminated water.⁵⁶ It has been described in homosexual men but there is no evidence that it is sexually transmitted.⁵⁷

Hepatitis G (GB virus, HGV, GBV-C)

Hepatitis G may be a misnomer as there is little evidence that this flavivirus causes hepatitis and it probably does not replicate in the liver.^{58 59} It is prevalent throughout the world, causes chronic infection in about 50%, and is frequently found as a co-infection with hepatitis C and hepatitis B.^{58 59} Although this virus is mainly spread by the parenteral route, there is evidence that it may also be transmitted by the sexual route at an unknown rate and vertically (mother to infant) in up to 60% of infants.^{60 61} Until the pathogenic potential of this organism has been defined it will remain of diagnostic interest only in a research setting.

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